REMARKS

Claims1, 5, 17, 20, and 24-25 and 27 are pending in the subject application.

Rejection of claims 1, 5, 17, 24 and 27 under of 35 U.S.C. §112, First Paragraph

All pending claims stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. In particular, the examiner maintains that a skilled artisan would require some sort of correlation between the expression of EGFR levels in primary and metastic tumor for EGFR and that "[o]ther than the marker TS, one of skill in the art would not find such correlation" thus requiring undue experimentation to practice the claimed method.

A. Background: Enablement Requirement

The enablement requirement of § 112, ¶ 1 is set forth as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms *as to enable any person skilled in the art* to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § 112, ¶ 1 (1994) (emphasis added). The Federal Circuit has interpreted this paragraph of the stature to contain an "enablement" requirement distinct from the written description. *Vas-Cath v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1117 (Fed. Cir. 1991) (recognizing the severability of the "written description" and "enablement" provisions of § 112, ¶ 1). The standard for enablement is whether one skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. The Federal Circuit has further determined that compliance with the enablement requirement is a question of law based on underlying factual findings. *In re Vaeck,* 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

B. The pending claims are sufficiently described in the specification to allow the skilled artisan to use the method.

The Examiner's assertion that the specification must provide a correlation between the primary and metastatic tumors of the claimed tumor gene determinant before one of skilled in the art could determine the treatment of the metastatic tumor is contrary to the teaching of the specification. The present invention provides a method to determine an appropriate chemotherapeutic regimen for treating metastatic tumors based upon the level of

tumor gene expression from a patient derived primary tumor sample, regardless of the type of sample. (*See*, for example, page 10 lines 8-13 and page 22 of the specification). The passage of the specification cited by the Examiner as highlighting the need for some sort of correlation between the expression of EGFR level in a primary tumor as compared to that from metastatic tumors is actually a summary of the limitations of previous methods to quantify gene expression in primary tumor samples. (See page 8, lines 16-page 9, lines 12). Further, this section of the specification provides support for the present invention as it illustrates that contrary to the teachings of the present application, archived primary tumor tissue (especially fixed and paraffin embedded tissue) was thought to be ill suited for gene expression. (See page 10, lines1-7).

In particular, the present invention provides a method to determine the level of EGFR expression from a patient derived primary tumor sample. Moreover, the present invention provides a method to determine the level of EGFR expression from a patient derived primary tumor sample that is fixed paraffin-embedded tissue. (See, for example, page 24 lines 9-page 25, line 11). Additionally, the specification provides a sample uncorrected gene expression for EGFR, and further normalizing UGE with known relative EGFR expression levels can be calculated using the equations as provided in Example 3 of the specification. Additionally, on page 29 of the specification, the determination of the corrected relative ECFR expression is provided.

Further, Applicants have adequately provided in the specification that expression levels between primary tumors and metastatic tumors are similar. In particular, the specification provides proof of principle of the method as demonstrated by the detection of TS expression in primary tumors and metastatic tumors. This method that includes TS expression detection in primary tumors exemplifies the method for one species; there is no need to provide examples for every species. Moreover, the claims only require measuring primary samples to determine a chemotherapeutic regimen for treating a metastatic tumor based on the primary tumor expression level. Therefore, one skilled in the art can perform the claimed method without undue experimentation.

Applicants submit that the claimed method is adequately described in the specification to enable one skilled in the art to practice the method. Accordingly Applicants respectfully request withdrawal of this ground of rejection.

CONCLUSION

It is believed that the present claims are in conditions for allowance and earnestly request allowance. Extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefore (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 11-0600. The Office is hereby authorized to charge any additional fees or credit any overpayments under 37 C.F.R. 1.16 or 1.17 to Kenyon & Kenyon Deposit Account No. 11-0600. The Examiner is invited to contact the undersigned at 202-220-4258 to discuss any matter concerning this application.

Respectfully submitted,

KENYON & KENYON LLP

Date: 3/20/06

Teresa A. Lavenue
Reg. No. 47,737

1500 K Street, N.W.
Washington, D.C. 20005
Telephone: (202) 220-4200
Facsimile: (202) 220-4201